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GENETIC TESTING – PRESENT AND FUTURE PROBLEMS

The sequencing of the human genome has produced a huge quantity of genetic data. Nowadays scientists concentrate on applying this new information to clinically useful purposes and therapies. Genetic tests are considered to be one of the first applications.

A genetic test is the analysis of human DNA, RNA, chromosomes, proteins and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes or karyotypes for clinical purposes.[1] Depending on the test substance and the results that could be obtained, various testing methods are employed,[2] namely:

a) direct testing: the direct study of genes (DNA sequences) and RNA; this method is used to detect the disease caused by an identified well-known mutation; these changes can be easily found and interpreted,
b) linkage testing (indirect testing): is used when the gene cannot be identified directly, but the region of chromosome is known; application of the method requires additional DNA testing of several relatives of the tested person, in order to find the presence of pathogenic changes (mutations) in the gene by identifying genetic markers of DNA that are inherited together with the tested genes,
c) biochemical testing: an examination of some metabolites, such as enzymes or proteins; enzymatic analysis measures the rate of chemical reaction in the presence of a protein that facilitates the reaction (enzyme); the activity of the enzyme is quantified in order to diagnose genetic disease; by analysis of the proteins one can study the modifications in the structure of a protein, which may be caused by the change in the gene encoding the protein data,
d) cytogenetic testing: an examination of chromosomes.

Application of genetic testing can be divided into two groups: non-medical and medical. The most frequently mentioned field of use of genetic testing for non-medical purposes are insurance and employment. The present paper concentrates on the medical purposes of genetic testing.

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[1] W. Burke, *Genetic testing* , "The New England Journal of Medicine" 2002, vol. 7, pp. 1867–1875; N. Holtzman et al., *Promoting Safe and Effective Genetic Testing in the United States: Final Report of the Task Force on Genetic Testing*, Johns Hopkins University Press, Baltimore 1999.

[2] http://www.genetests.org/servlet/access

Medical uses of genetic testing are as follows:[3]

- Pre-implantation testing,
- Prenatal testing,
- Carrier testing,
- Newborn screening,
- Diagnostic testing,
- Predictive and presymptomatic testing.

Pre-implantation testing

Pre-implantation genetic diagnosis is used to detect a particular genetic or chromosomal disorder in embryos that were created using assisted reproductive techniques such as in-vitro fertilization.

Prenatal testing

This type of testing is used during pregnancy to detect certain genetic disorders (in the genes or chromosomes) in the foetus.

Carrier testing

Carrier testing is performed to identify a person who carries one copy of a gene mutation that, when occurs in two copies, causes a genetic disease. They usually do not have symptoms related to the gene mutation. Individuals can have various kinds of disorder caused by a gene mutation, which is inherited in:

1. Autosomal recessive manner – disorders, such as cystic fibrosis and Tay-Sachs disease. Carriers can be either males or females.
2. X-linked recessive manner – disorders, such as Duchenne muscular dystrophy or hemophilia A. Carriers are only females. They have one of the two X chromosomes which possess a defective gene.

Carrier testing is offered to individuals who have family history of genetic disorder and to individuals in ethnic or racial groups, which are known to have a higher carrier rate for a particular condition. The main purpose of this type of test is to provide future parents the information about risk of genetic disease for their offspring.

Newborn screening

This kind of testing is used to test all newborns for the early detection and implementation of the therapy of genetic disease. Currently in Poland all infants are tested for phenylketonuria, congenital hypothyroidism and cystic fibrosis. Each of these genetically conditioned diseases if untreated from birth cause irreversible effects on growth of a child's body.

Diagnostic testing

Genetic tests allow to exclude or confirm diagnosis, when one of the known genetic disorder is suspected.

Predictive and presymptomatic testing

The predictive and presymptomatic tests are used to detect gene mutations associated with disorders that appear later in life. Many of the diseases have both genetic and environmental etiology. Tests for late onset disorders depending on the type of disease may perform different functions:

[3] http://ghr.nlm.nih.gov/handbook/testing

- can unambiguously predict that a person will suffer a particular disease in the future. This is suitable for some diseases caused by single genes, such as Huntington's disease,
- can estimate the probability of the situation when someone will develop a particular disease in the future. This function is used in tests for Alzheimer's disease and some cancers.

The essential aspect of genetic tests are their predictive character. With the ability to know about our genetic condition we may better evaluate our health status in the distant future. Of course, the medical benefits of using genetic tests are uncontested despite the fact that genetic tests have provoked debates about possible negative effects. The most frequently mentioned controversies are introduced briefly in the following sections of the present paper.[4]

Free consent

There is no doubt that before performing any type of genetic test, free and informed consent should be guaranteed. However, expressing free and informed consent is not that trouble-free. The remaining problem is how to treat the consent of minors and persons with intellectual impairment.[5]

Besides that, questions are still open with assignment of the scope of consent. Samples of biological material derived from a human being (e.g. cells, blood, DNA) can be stored in the so-called biobanks. Samples are linked to personal data and information about their donors. It is obvious that such a huge database can help to identify the causes and mechanisms of numerous diseases.[6] However, many researchers have concluded that these opportunities are reduced by a strict concept of consent. Recently, the main solution to this problem is to ask the donors for permission for every new use of material or data. Most of the existing regulations of biobanks state that the explicit consent of the donor may be waived under certain conditions, such as anonymous samples and data, or restricted to a specific type of research but this is still an unsatisfactory solution as the sample and the data are limited to certain applications. Lately, some voices have called for the introduction of general consent, so that donors would give permission for any use of their genetic information.

While discussing the issue of freedom of choice, aspects of social and economic pressure also must be taken into account. The reasoning for this position is that the representation of illness, disability and care options may introduce subjective limits for freedom of choice. This is particularly the case when pre-

[4] *Ethical and Social Aspects of Genetic Testing Services: Issues and Possible Actions,* http://www.eurogentest.org

[5] *Genetic Testing in Asymptomatic Minors: Recommendations of the European Society of Human Genetics*, "European Journal of Human Genetics" 2009, vol. 17, pp. 720–721; doi:10.1038/ejhg.2009.26.

[6] B. Godard et al., *Data Storage and DNA Banking for Biomedical Research: Informed Consent, Confidentiality, Quality Issues, Ownership, Return of Benefits. A Professional Perspective*, "European Journal of Human Genetics" 2003, vol. 11, Suppl. 2, S88–S122.

natal diagnosis and genetic tests are offered to people with a family history of disease. Screening programs may also increase the social pressure for patients. An example might be a neonatal screening: while now parents may refuse it, in the future they would not really have a choice, because it would have become standard practice.

Access

Genetic testing services are projected to be an integral part of the health care system offered. Therefore, it seems clear that genetic tests should be available to anyone, without considering the status, income or place of residence of a person, although it does not mean that genetic testing must be available without control and restrictions. Fundamental conditions, such as the proper genetic counselling, must be fulfilled in order to minimize the problems and risks associated with widespread use of genetic testing.[7] It is postulated that genetic testing must be affordable and inexpensive otherwise it may cause inequality in society. Nowadays there are more and more concerns about the patenting of genes with some warning that gene patents may be a potential barrier for the development of genetic studies, and may also limit access to genetic testing.[8] Geneticists are not opponents of gene patents as such, but they oppose the creation of a monopoly by asserting rights over the sequences of genes and its mutations.[9] They argue that it is necessary to change provisions and period of compulsory licensing. Regulations on access to genetic tests and their quality should be standardized.

While discussing the availability and quality of genetic testing the important role of physicians should be noted.[10] The results of studies have showed that doctors' understanding and awareness about genetics and genetic testing varies widely in different countries. As a result, the patients obtained different information about the availability of genetic testing, the treatment options and the results of the genetic tests. Contemporary, widely used genetic tests have been developed as technically simple and easy to apply and genetic testing can be performed by people without medical qualifications. The leading view on the matter is that only competent persons should conduct genetic tests.[11] It is assumed to be the only way to provide the high quality of the services and to ensure the appropriate psychological support for patients. The information given by a physician before, during and after the genetic testing is considered to be the

[7] *Recommendations for Genetic Counseling Related to Genetic Testing,* http://www.eurogentest.org.

[8] E.M. Kane, *Patent-Mediated Standards in Genetic Testing*, "Utah Law Review" 2008, p. 835.

[9] A. Lecrubier, *Patents and Public Health. EMBO reports* 3, 12, 1120–1122 (2002); doi:10.1093/embo-reports/kvf25.

[10] J.C. Knight, *Genetics and the General Physician: Insights, Applications and Future Challenges*. "QJM: An International Journal of Medicine" 2009, vol. 102, pp. 757–772; doi:10.1093/qjmed/hcp115.

[11] http://www.eurogentest.org

most important thing in evaluating the quality of the service. However, in some cases it is difficult to determine whenever about the genetic status will do more harm than good to a patient. The key moment in genetic testing is high quality advice provided by the physician and this must depend strongly on the patient individuality, because some patients just want to rely on their doctors, while others require detailed description of the test and its consequences. Some scientists believe that patients themselves should determine the amount of information they want to receive.

The right to know or not to know

Every human being has the right to obtain genetic information associated with his or her present or future health status. It is considered to be the right to know which is the key patient right. At the same time, every person has the right not to know about the probable genetic "scenario" of his or her life. Some scientists believe that for some groups of patients affected by certain disorders, there should be a right not to know when a treatment is not available.[12] Some of them go even further and argue that no genetic testing should be offered when the treatment is not available.[13] Such views are negated by those who believe that even if treatment is not available, the knowledge alone can still be desired.[14] The information provided by genetic tests can help someone to reduce the risk of a probable disease, as well as to make important, conscious decisions about future life.

Both the right to know and the right not to know must be expressed by a patient. The first appears as a fundamental patient right related to medical practice, while the second refers to the freedom of choice.

Privacy

Genetic tests may provide very important information about the health and specific characteristics of the person. Consequently, the fundamental question in the discussion about genetic testing is the issue of privacy.

An important place in the debate over privacy is the status of genetic information and there are two opposing views. The first is that genetic information is not different from any of the other patient's data and the protection of such data is sufficient. The second view suggests that the results of genetic tests provide

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[12] L. Hennen et al., *Genetic Diagnostic – Status and Prospects*, Status report, TAB Working report, No 66, Berlin 2000.

[13] *Ibidem*.

[14] A. Kent, *We Can Change the Future*, EMBO Rep. 2005, September, 6 (9), pp. 801–804; doi:10.1038/sj.embor.7400513.; de Melo-Martín, Inmaculada. *Genetic Testing: The Appropriate Means for a Desired Goal?*, "Journal of Bioethical Inquiry" 2006, vol. 3, no. 3, December.

much more information about patients and their families than other medical tests and, as a result, genetic information should be subjected to rigorous data protection rules.

There is no doubt that genetic information concerning private persons should be specially protected because of its special character. The transmission of such information should always be anonymous and it is a reasonable point of view that the potential use of genetic information may be made only after obtaining unambiguous consent of that person for it. The problem arises when discussing the transfer of genetic data to private organizations or private research institutes.

Privacy is an important issue associated with the development of pharmacogenetics. It is envisaged that in the near future more and more genetic tests assessing the body's response to a specific drug will appear. The use of such tests will allow the application of the most appropriate pharmacotherapy for the individual and, consequently, speed up and improve the treatment of diseases. An important issue is that from the sample for a pharmacogenetic test it is not only information about the sensitivity to study medicine that can be collected but also other genetic information. If the tests "made to measure drugs" are routine, it will be easy to obtain knowledge about the other patient's genetic traits, which may lead to the dissemination of genetic information and a threat to patient privacy.[15]

The issue of privacy frequently appears when discussing the protection of genetic samples in biobanks created for research purposes. It is complicated to establish the level of data protection to be achieved in biobanks for genetic research. Some argue that strict data protection is required, while others believe that too severe regulation may create barriers to research and should thus be avoided.

The largest part of the information that can be obtained by using genetic tests also usually concerns information about person's relatives. Due to that fact a number of questions arise.[16] The most important of them are: are people with genetic disorders obliged to inform their relatives that (they may) have the same disorder in the genome; what should be done when someone does not want to inform relatives and who bears the responsibility for not telling relatives? This dilemma can be solved in several different ways. In some countries, for instance, the law states that doctors are not allowed to reveal genetic information to patients' relatives yet they have to inform their patients about the meaning of the information for their relatives. The patient ought to decide whether tell them or not but, on the contrary, there are regulations relating to genetic analysis which allow physicians to provide information to the person's relatives, if this information could influence their health status.

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[15] D. Melzer et al., *Genetic Tests for Common Diseases: New Insights, Old Concerns*, "British Medical Journal," 15 March 2008, vol. 336.

[16] K. Douglas et al. (2009). Public Perceptions of Ethical Issues Regarding Adult Predictive Genetic Testing. Health Care Anal.DOI 10.1007/s10728-009-0113-4.

Commercialization

The increasing accessibility of genetic testing techniques and the progressively lower cost of research is causing the commercialization of genetic tests.[17,18] New companies are being formed, offering personal whole-genome information services, even via the Internet. Currently, for the fee of about US$400,[19] individuals can buy online access to their personal genetic information collected from a previously sent saliva sample.[20] Most of the companies offering such services are based in the United States.

Discrimination

The issue of discrimination engages an important position in the debate on genetic testing since genetic studies may strengthen existing discrimination in some societies. Some groups of people can actually feel discriminated by the fact that genetic tests are offered for the condition that they have. It is also worth mentioning the risk related to the origin of racial and ethnic discrimination, mainly linked to screening programs carried out on certain ethnic groups which have a high probability of developing certain diseases.[21]

Numerous concerns have been raised about the use of the results of genetic tests by insurance companies.[22] It seems that the use of genetic tests results could lead to the discrimination of people based on their health status. The main concern stems from the prospect of the wide use of genetic tests in determining the potential risk of certain diseases in order to evaluate insurance premiums. As a result, for certain groups, private insurance would become impossible or very expensive. In parallel with the fear of discrimination by insurance companies, the question of discrimination by employers demanding genetic information from their employees arises. The concern emerges that an employer can refuse employment to people in groups at risk of certain diseases but those fears seem to be unfounded.

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[17] S. Hogarth et al., *The Current Landscape for Direct-to-Consumer Genetic Testing: Legal, Ethical, and Policy Issues*, "Annual Reviews of Genomics and Human Genetics" 2008, vol. 9, pp.161–182.

[18] J. Kaye, *The Regulation of Direct-to-Consumer Genetic Tests*, "Human Molecular Genetics" 2008, October 15, 17(R2) R180–R183; doi:10.1093/hmg/ddn253.

[19] https://www.23andme.com

[20] J.A. Robertson, *The $1000 Genome: Ethical and Legal Issues in Whole Genome Sequencing of Individuals*, "The American Journal of Bioethics" 2003, vol. 3 (3).

[21] M.J. Khoury et al., *Population Screening in the Age of Genomic Medicine*, "The New England Journal of Medicine" 2003, January 2.

[22] B. Godard et al., *Genetic Information and Testing in Insurance and Employment: Technical, Social and Ethical Issues*, "European Journal of Human Genetics" 2003, vol. 11, Suppl. 2, S123–S142.

Genetic tests in particular are different from conventional methods of medical diagnosis due to the fact that may be used for selection. Two types of selection can be distinguished: negative and positive. The first prevents the conception regarding to definite medical indications, the second selects individuals with certain genetic traits. The debate about negative selection is closely related to pre-implantation tests and there are a number of different viewpoints on this topic. Some argue that usage of pre-implantation tests should be prohibited because it means the manipulation of life. Some experts have a much more liberal point of view and, according to them, there should not be any restrictions on the availability of pre-implantation tests. Whether to do pre-implantation diagnosis or not is an individual choice. Even more controversial is positive selection – the use of pre-implantation testing for selecting an embryo which has desirable genetic traits.

Conclusion

Recently the progress of genetics has been so enormous that sometimes it is difficult to tell what is really possible and what is only probable in the near future and genetic tests are one of these ambiguous issues.

Knowledge about the interactions between genes and disease is rapidly increasing and there are currently genetic tests for more than 1,300 diseases. Genetic testing is getting cheaper, faster and more common. However, the fact that frequent conditions, for instance heart disease, ensue from complex interactions between environmental and genetic factors should be taken into consideration as well.

To conclude it is worth mentioning that even though genetic testing has much in common with other types of laboratory testing, it is exceptional and requires special consideration. How to use and regulate this new information for the benefit of society requires active debate.